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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/036,308	10/26/2001	Eleftherios P. Diamandis	11757.58USU1	2749

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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	7

DATE MAILED: 04/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/036,308	DIAMANDIS, ELEFTHERIOS P.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 6 is acknowledged. The traversal is on the ground(s) that claims 7-10 depend from claims of Group I and, therefore, could be examined together. This is found to be persuasive and claims of Groups I and II have been rejoined.

Claims 14-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

Claims 1-13 are under examination in the instant office action.

Claim Objections

2. Claims 1, 2, 4, 5 and 6, are objected to because of the following informalities: terms "Alzheimer's disease" and "Alzheimer's Disease" are used in the claims interchangeably. Applicant is advised to use similar terms throughout the text of the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing Alzheimer's disease in a subject comprising detecting the specific levels of hK6 in a sample of whole blood or cerebrospinal fluid, does not reasonably provide enablement for a method for diagnosing and monitoring Alzheimer's disease in a subject comprising detecting hK6 in a sample derived from a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-13 are broadly drawn to a method for diagnosing and monitoring Alzheimer's disease in a subject by detecting hK6 in a sample derived from the subject. hK6, human kallikrein 6, is a serine protease (also known as zyme, protease M or neurosin), which has recently been discovered to be present in many biological fluids and tissues. The instant specification discloses the results of the measurement of the concentration of hK6 in different samples of normal and pathological origin. It is clear from Table 2 (page 23 of the instant specification) that the concentration of hK6 in CSF and whole blood samples of patients with Alzheimer's disease (AD) was significantly higher than in normal control samples. Thus, by detecting specific levels of hK6 in CSF and whole blood, a diagnosis of Alzheimer's disease can be made. However, the instant specification does not provide enablement for a method that allows diagnosis and monitoring of Alzheimer's disease by detecting the presence of hK6 in any sample, thereby requiring undue experimentation to discover how to use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

It is known from the prior art that hK6 (or zyme) is expressed predominantly in brain, kidney, and salivary gland (Little et al., J. Biol. Chem., 1997, Vol. 272, No. 40, pp.25135-25142, specifically the abstract and the last paragraph of page 25135). Thus, based on this information and the information provided in the instant specification (see page 22, Table 1 and page 23, Table 2), one skilled in the art would reasonably conclude that mere detection of hK6 in any biological sample derived from the subject would not provide for diagnosis of Alzheimer's disease because it is clear that hK6 can be present in plurality of fluid and tissue samples.

Moreover, the same publication of Little et al. at page 25135 clearly discloses that hK6 can be detected in normal and AD adult brain. Ogawa et al. (Psychiatry and Clin. Neurosci., 2000, August, 54, pp.419-426) describe the results of immunostaining of brain slices with the antibody to neurosin (hK6), which showed positive staining in normal control and Parkinson's disease cases. Finally, Table 2, page 23, of the instant specification presents the data, which plainly indicate that both normal and AD samples of whole blood, frontal cortex tissue extract and SCF contain hK6. Therefore, a skilled artisan would rationally assume that because hK6 is present in normal samples as well as in AD and Parkinson's disease samples, detecting hK6 in a biological sample would not lead to diagnosis of AD.

Further, the instant specification fails to provide any information on how to monitor Alzheimer's disease by the claimed method. There is no discussion or any other indication that

the findings of high concentration of hK6 in blood and CSF samples of AD patients were estimated based on the level of progression of AD. In the absence of teachings or working examples in the instant specification for this particular limitation, and in view of the lack of information found in prior art, a skilled artisan would have to resort to a significant amount of undue experimentation in order to discover how to practice Applicant's invention as currently claimed.

Finally, claim 5 in section (c) and claim 6 in section (d) recite a step where quantitated level of hK6 is compared to levels of hK6 in other samples of the subject. According to the data in Table 2, lines 1 and 5, the amount of hK6 can be apparently similar between different samples obtained from AD subjects. Again, due to the lack of information in the known literature regarding the levels of hK6 in different biological samples derived from patients suffering from AD, and in view of the data presented in Table 2 of the instant specification, one skilled in the art would reasonably conclude that substantial undue experimentation is necessary to determine how to practice the claimed method when comparison between different samples has to be made.

Thus, in view of the lack of teachings and examples in the instant specification and unpredictability of the art as set forth earlier, the instant specification is not found to be enabling for the full scope of a method for diagnosing and monitoring Alzheimer's disease by detecting hK6 in a sample. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to practice Applicant's invention commensurate in scope with the instant claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 is vague and indefinite in so far as it employs the term "hK6". This term should be identified by its full name followed by the abbreviation at its first occurrence in the text of the claims. Appropriate correction is required.

6. Claims 1-3 and 5-6 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claims 1-2 encompass a method without any method steps. Claims 3 and 5-6 omit the essential step that leads to diagnosing and monitoring of Alzheimer's disease. Claims 3, 5 and 6 in sections (b), (b) and (c), respectively, also omit the step of quantification of hK6. Note, that detection of hK6 in a sample does not equal to the quantification of hK6 in a sample.

7. Claim 4 is vague and indefinite for recitation "a level of hK6 greater than". "Greater" is a relative term, therefore, the metes and bounds of the recitation cannot be determined from the claim or the instant specification unless the specific level or degree of the difference is clearly defined.

8. Claims 3 and 4 are further vague and ambiguous for reciting "a standard". The claimed method appears to encompass a quantitative assay wherein the determination of very specific levels of hK6 leads to diagnosis of AD. Therefore, the term "a standard" should be defined by precise levels of the amount of hK6, which are indicative of AD.

9. Claims 7 and 8 recite the limitation "the biological sample" in claim 2. There is insufficient antecedent basis for this limitation in the claim.

10. Claim 13 recites the limitation "hK6 is measured" in claim 5. There is insufficient antecedent basis for this limitation in the claim.

11. Claims 10, 11 and 12 are indefinite for being dependent from indefinite claims.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original

signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. OC
April 4, 2003

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